

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANT: William J. Curatolo et al.

SERIAL NO.: 09/770,562

FILED: January 26, 2001

FOR: Solid Pharmaceutical Dispersions
with Enhanced Bioavailability

Examiner: B. Fubara
Art Unit: 1618

Commissioner for Patents
Washington, D.C. 20231

Sir:

DECLARATION UNDER 37 CFR 1.131

I, James A.S. Nightingale, declare that:


1. I was awarded the degree of Bachelor of Science in Chemical Engineering in 1980 by the University of Washington, Seattle, Washington, a degree of Master of Science in 1986 in Bioengineering by the University of Washington, Seattle, Washington, and a Ph.D. in 1988 in Bioengineering by the University of Washington, Seattle, Washington.
2. Prior to being employed with Bend Research I was employed from 1988-1993 as a Staff Scientist by Ciba-Geigy Corporation, Pharmaceuticals Division, Ardsley, New York where my areas of expertise included transdermal drug-delivery research and the development of second-generation transdermal pharmaceutical products; and from 1980-1988 as a Research Assistant for the University of Washington, Seattle, Washington, where my areas of emphasis included biomaterials, polymer synthesis and characterization, organic chemistry, biochemistry, and chemical engineering.

3. I have been employed by Bend Research, Inc., of which I am also a part owner since 1993. My title is Director, Pharmaceutical Research.
4. Bend Research, Inc. is part-owned by Pfizer, Inc., the Assignee of the above-identified application.
5. I am an inventor of the instant patent application.
6. I have reviewed the examples in the instant application. In particular attached to this declaration as Exhibit A are notebook pages relating to work I supervised in connection with the process used to form solid amorphous dispersions of a drug and hydroxypropylmethyl cellulose acetate succinate (or HPMCAS), as well as Examples 25 and 26 of the instant application. The notebook pages show that drugs were spray dried with HPMCAS to form solid amorphous dispersions. The dates on the notebook pages have been redacted. However, these examples were made prior to February 13, 1997.
7. I further declare that all statements made herein of my own knowledge are true and that all statements made on information are believed to be true; and further that these statements were made with the knowledge that willful false statements and the likes made are punishable by fine or imprisonment or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Respectfully submitted,

24 May 2007

Date

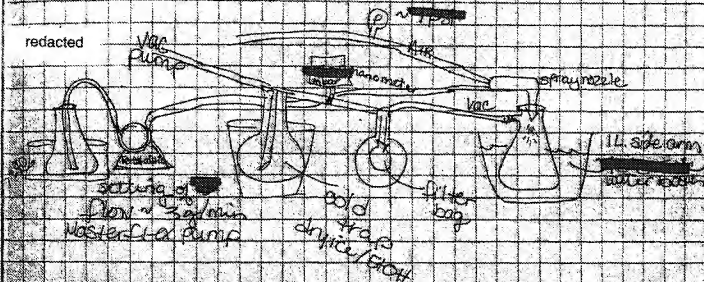

James A.S. Nightingale

G:\BRI Corporate\Legal\Patent\PC 9574 HPMCAS SDDs\JASN Declaration 3-1-07.doc

TITLE

From Page No. _____

Making spray dried solvent dispersion.
This is the set-up



filter bag - paper towel rubber banded to the inner part of the trap

Masterflex pump - head 1013-20 tubing 1404-1C

note also of RP 4386 + 1404-1C - see pg 15 for results

To Page No. _____

Witnessed & understood by me:

Date

Invented by

Date

Joel E. Baker

redacted

Recorded by

Chad Hostetter

redacted

Project No. _____

Book No. _____

77

TITLE

From Page No. En's / HPMCAS spray-dried disp (1:10)

1800mg HPMCAS

200ml Acetone

200mg En's

38°C

Heated Acetone, added HPMCAS when no clumps, added En's

T₀ = 3:20pm redactedH₂O = 45-55°CT₀C = 440mmbar

pump setting = 3 (~3ml/min.)

air pressure = 10psi

and 6:20pm

Tested @ Day 1 - Data on pg 1320-83 looks good!

To Page No. _____

Witnessed & Understood by me,

John E. Barker

Date

redacted

Invented by

Recorded by

John E. Barker

Date

redacted

TITLE

Project No. _____
Book No. 330

From Page No.

See 1330-79

Answer: 1:2 + 1:5 Dispersions, 21 after vacuum drying overnight.

For 1:2 \Rightarrow 4.01mg / 10ml \Rightarrow 200.5 μ g/ml
1:5 \Rightarrow 10.02mg / 10ml \Rightarrow 200.4 μ g/ml

Grise/UV/vis/absorption/absorption aux										Sheet1		Date: 13/05/03	
Resolution Testing										Printer:		13/05/03	
Resolution Testing										Analyst:		CL Horvath	
RECEPTOR SOLUTION: 10ml of 50% H ₂ O/POPC/H ₂ O, pH 6.5.													
DRUG: Griseofulvin/HMCAAS spray-dried Dispersion													
Theoretical max. concentration: 200 µg/ml													
Dilution of (1:10) 90% Griseo/10% HMCAAS spray-dried dispersion, Day 1													
HPLC ANALYSIS													
CIL column (Phenomenex, Ultrasorb)										Standard Factor:			
300/0.0 0.03M H ₂ PO ₄ -pH5.0/ACN										Y-INT: 11.47534137 SLOPE: 17.3269122			
A. Peak-1				B. Peak-2				C. Peak-3					
min	area	PPM	auc	min	area	PPM	auc	min	area	PPM	auc		
0	0	0	0	0	0	0	0	0	0	0	0		
0.5	873.47	64.184123	25.547203	0.5	698.37	76.020594	10.76554101	0.5	654.75	74.1807118	11.54545278		
1	3495.17	171.026267	620.530005	1	5441.47	165.050426	568.33930076	1	5438.54	129.745238	560.034456		
50	1521.65	174.815168	4940.48904	50	1837.55	187.670445	4876.075792	50	1678.56	162.310022	5047.54691		
90	1818.16	174.832627	7104.652203	90	1498.37	177.823547	10992.5592	90	1567.29	178.963691	10934.4474		
120	1564.03	126.29372	20993.83005	120	1493.19	168.412184	20956.3733	120	1593.29	144.714397	20336.3775		
180	1459.54	177.757692	61346.6205	180	1820.23	150.709399	81072.51808	180	1465.01	159.292522	29749.6386		
1200	10222.94	715.339187	315162.4771	1200	11618.75	150.856427	302821.418	1200	10359.1	110.847434	174992.061		
D. Filter-1				E. Filter-2				F. Filter-3					
min	area	PPM	auc	min	area	PPM	auc	min	area	PPM	auc		
0	0	0	0	0	0	0	0	0	0	0	0		
0.5	159.72	71.81595195	25.4957961	0.5	710.69	81.554465	30.17133693	0.5	784.19	50.7684091	22.4421077		
1	1620.23	183.282271	622.88357	1	5474.80	184.318112	595.3703183	1	1028.39	151.646032	505.400174		
50	1457.35	166.992918	4752.8375	50	1550.39	177.022635	4811.5332628	50	1612.24	173.229324	4825.09588		
90	1613.76	174.02683	6522.73695	90	1834.38	172.003561	10504.10635	90	1474.37	156.557878	8751.90452		
120	1420.82	169.022239	13948.8919	120	1502.34	172.003561	20504.10635	120	1425.97	163.27405	18706.7864		
180	1495.02	171.59141	28934.5313	180	1495.56	172.011863	28987.3205	180	1439.83	164.816286	29549.7051		
1200	107.03	97.626758	104229.131	1200	1120.91	138.09813	154307.11	1200	1165.08	158.496104	132695.056		

Time (min)

— **Frank** —

1135K-2

—1984—

— 34 —

100%

Witnessed & Understood by me.

Date _____

Invented by

Date _____

To Page No.

redacted

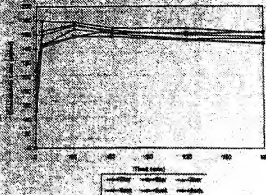
Recorded by _____

redacted

1:4 Erisedulvin / NMCAS

500mg GNS 22.50ml
20g 4AmCAS 1000ml

and - when I come back in the room I checked on the spray, the filter must have been plugged because the spray needle stop had "popped" & wasn't sealing, but the vacuum was still reading 300mm. There wasn't much liquid left in spray, so I turned off the feed pump. I let the dispersion dry as much as possible. When recovering the dispersion - it looked OK - not used, I still vacuum-dried it overnight anyway.

[illegible]

To Page No.

Date redacted

Recorded by _____